REMARKS

Applicant has amended the specification to correct typographical error in a sequence referred to as ODN1585 (SEQ ID No. 12). The sequence appeared in its correct form in the sequence listing. Nucleotide No. 15 of SEQ ID No. 12 appears on page 22 of the specification as a C rather than a G. This error was typographical in nature and correction of it does not constitute new matter.

Substitute sheets for pages 38 and 47 have also been submitted herewith. It was noted in the Office Action (paper no. 9, page 1) that informalities were found on page 38 and page 47 in which two lines were illegible. Applicant has corrected these informalities by submitting substitute sheets. On page 38, the last line (following the line beginning with "1842") has been re-written in a legible form. No other changes were made to the text on page 38. On page 47, the fourth line after the table was re-written in a legible form. No other changes were made to page 47. No new matter is added by these corrections.

Claim 1 has been cancelled and is no longer being pursued in the above-identified patent application. Claim 47 has been amended to remove the language "occurs at the 3' end of the nucleic acid" and to replace it with the language --is selected from the group consisting of a phosphorothioate and a phosphorodithioate modification--. No new matter is added by this addition. New claim 54 has been added. New claim 54 is similar to pending claim 42 except that the size limitation has been removed and the limitation that the nucleic acid contain a phosphate backbone modification has been added. New dependent claims 55-58 have been added. Support for claims 55 and 57 which relate to the oral, transdermal, or subcutaneous administration of CpG oligonucleotides is found at least in the specification on page 54, lines 9-10. Support for new claims 56 and 58 which relate to the administration of formulated (nucleic acid delivery complex, liposome, virosome, nanoparticle) CpG oligonucleotides is found in the specification at least on pages 18, lines 12-20, 37, lines 16-18, 51, line 32, and 54, line 13. No new matter has been added.

References

Applicant submits herewith copies of references which were previously cited on Form PTO-1449 and which were not considered because copies could not be identified in the parent files. It is indicated in the Office Action (paper no. 9) that Applicant could submit copies of the indicated references in response to the Office Action without the submission of any fee for such consideration.

Rejection of Claim 47 Under 35 U.S.C. §112

Claim 47 has been rejected under 35 U.S.C. §112, second paragraph, as being indefinite because of the language "phosphate backbone modification of the 3' end of the nucleic acid".

Applicant has amended claim 47 to remove the cited language. An additional limitation that the phosphate backbone modification is either a phosphorothioate or a phosphorodithioate modification has been added. The additional limitation was added so that claims 47 and 46 do not have the same scope.

Rejection of Claims 42-53 Under 35 U.S.C. §112, first paragraph

Claims 42-53 have been rejected under 35 U.S.C. §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention". The basis for the rejection is that the "application gives no data relevant to the use of the nucleic acids mentioned in the claims in any *in vivo* method to effect the change mentioned in the claims". Applicant respectfully disagrees.

Claims 42-53 and new claim 54 all relate to a method for redirecting a subject's immune response from a Th2 to the Th1 immune response by administering a CpG containing nucleic acid. The specification as filed includes both *in vitro* and *in vivo* data demonstrating that CpG nucleic acids redirect an immune response from a Th2 to the Th1. Several *in vitro* studies demonstrate the preferential induction of Th1 cytokines. For example, page 41, lines 1-22, describe a study on human PBMC examining the induction of IL-12 in response to CpG ODN. The specification teaches that IL-12 secretion is a good measure of the ability of a compound to

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produce a Th1 immune response and function as an adjuvant. Figures 13 and 14 showed the results of *in vivo* studies that demonstrate that CpG shifts Th2 to a Th1 immune response. Figures 13 and 14 are described on page 12, lines 17-25 and pages 64-65. Lines 1-5 of page 65 recite the following. "Figure 13 shows that the resultant inflammatory response correlates with the levels of the Th2 cytokine IL-4 in the lung. Figure 14 shows that the administration of an oligonucleotide containing an unmethylated CpG motif can actually redirect the cytokine response of the lung to production of Il-12, indicating the Th1 type of immune response." Thus, when a condition which ordinarily raises a Th2 immune response (such as that shown in Figure 13) is combined with a CpG ODN, the immune response shifts to a Th1 type. Thus, the application as filed provides both *in vitro* and *in vivo* data demonstrating that the CpG ODN are useful for redirecting a subject's immune response from a Th2 to the Th1.

Rejections of Claim 1

Several rejections of claim 1 have been raised. Applicant has cancelled claim 1. Claim 1 was only maintained in the case in order to have one claim pending at the time the divisional was filed. Applicant does not intend to pursue this claim in the above-identified patent application. Therefore, the rejections raised in the Office Action are not addressed with respect to claim 1.

Summary

Applicant has amended claim 47 and has addressed the rejection of the remaining claims. It is believed that all of the pending claims are now allowable. If the Examiner has any questions or comments, he is encouraged to contact Applicant's representative at the number listed below.

Respectfully submitted,

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